Claims

We claim:

1. A targeting construct comprising:

(a) a first polynucleotide sequence homologous to a target gene, wherein the target gene a lymphoid-specific GPCR gene;

(c) a second polynucleotide sequence homologous to the target gene; and

(d) a selectable marker.

2. The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.

3. A method of producing a targeting construct for a lymphoid-specific GPCR gene, the method comprising:

(a) obtaining a first polynucleotide sequence homologous to a lymphoid-specific GPCR gene;

(b) obtaining a second polynucleotide sequence homologous to a lymphoid-specific GPCR gene;

(c) providing a vector comprising a selectable marker; and

(d) inserting the first and second sequences into the vector, to produce the targeting construct.

4. A method of producing a targeting construct for a lymphoid-specific GPCR gene, the method comprising:

(a) providing a polynucleotide sequence homologous to a lymphoid-specific GPCR gene;

(b) generating two different fragments of the polynucleotide sequence;

(c) providing a vector having a gene encoding a selectable marker; and

(d) inserting the two different fragments into the vector to form the targeting construct.

5. A cell comprising a disruption in a lymphoid-specific GPCR gene.

6. The cell of claim 5, wherein the cell is a murine cell.

7. The cell of claim 6, wherein the murine cell is an embryonic stem cell.

8. A non-human transgenic animal comprising a disruption in a lymphoid-specific GPCR gene.

9. A cell derived from the non-human transgenic animal of claim 8.

10. A method of producing a transgenic mouse comprising a disruption in a lymphoid-specific GPCR gene, the method comprising:

(a) introducing the targeting construct of claim 1 into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse.

11. A method of identifying an agent that modulates the expression of a lymphoid-specific GPCR, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in a lymphoid-specific GPCR gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the expression of lymphoid-specific GPCR in the non-human transgenic animal is modulated.

12. A method of identifying an agent that modulates the function of a lymphoid-specific GPCR gene, the method comprising:

(a) providing a non-human transgenic animal comprising a disruption in a lymphoid-specific GPCR gene;

(b) administering an agent to the non-human transgenic animal; and

(c) determining whether the function of the disrupted lymphoid-specific GPCR gene in the non-human transgenic animal is modulated.

13. A method of identifying an agent that modulates the expression of lymphoid-specific GPCR, the method comprising:

(a) providing a cell comprising a disruption in a lymphoid-specific GPCR gene;

(b) contacting the cell with an agent; and

(c) determining whether expression of the lymphoid-specific GPCR is modulated.

14. A method of identifying an agent that modulates the function of a lymphoid-specific GPCR gene, the method comprising:

(a) providing a cell comprising a disruption in a lymphoid-specific GPCR gene;

(b) contacting the cell with an agent; and

(c) determining whether the function of the lymphoid-specific GPCR gene is modulated.

15. The method of claim 13 or claim 14, wherein the cell is derived from the non-human transgenic animal of claim 8.

16. An agent identified by the method of claim 11, claim 12, claim 13, or claim 14.

17. A transgenic mouse comprising a disruption in a lymphoid-specific GPCR gene, wherein the transgenic mouse exhibits cellular infiltration.

18. The transgenic mouse of claim 17, wherein the cellular infiltration is comprised of lymphocytes.

19. The transgenic mouse of claim 18, wherein the cellular infiltration occurs in any one of the following organs: lung, pancreas, stomach or liver.

20. The transgenic mouse of claim 17, wherein the transgenic mouse is heterozygous for a disruption in a lymphoid-specific GPCR gene.

21. The transgenic mouse of claim 17, wherein the transgenic mouse is homozygous for a disruption in a lymphoid-specific GPCR gene.

22. A method of producing a transgenic mouse comprising a disruption in a lymphoid-specific GPCR gene, wherein the transgenic mouse exhibits cellular infiltration, the method comprising:

(a) introducing a lymphoid-specific GPCR targeting construct into a cell;

(b) introducing the cell into a blastocyst;

(c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce the transgenic mouse comprising a disruption in a lymphoid-specific GPCR gene.

23. A transgenic mouse comprising a disruption in a lymphoid-specific GPCR gene, wherein the transgenic mouse exhibits at least one of the following phenotypes: peribronchiolar cellular infiltrates in the lungs; periductular cellular infiltrates in the pancreas; cellular infiltrates in the deep mucosa, submucosa, or muscularis of the stomach; or cellular infiltrates in the portal triads of the liver.

24. A cell derived from the transgenic mouse of claim 17, claim 22 or claim 23, wherein the cell comprises a disruption in a lymphoid-specific GPCR gene.

25. A method of identifying an agent that ameliorates cellular infiltration, the method comprising:

(a) administering the agent to the transgenic mouse comprising a disruption in a lymphoid-specific GPCR gene; and

(b) determining whether the agent ameliorates cellular infiltration in the transgenic mouse.

26. The method of claim 25, wherein the cellular infiltration is comprised of lymphocytes.

27. The method of claim 26, wherein the cellular infiltration occurs in any one of the following organs: lung, pancreas, stomach or liver.

28. A method of identifying an agent which modulates lymphoid-specific GPCR expression, the method comprising:

(a) administering an agent to the transgenic mouse comprising a disruption in a lymphoid-specific GPCR gene; and

(b) determining whether the agent modulates lymphoid-specific GPCR expression in the transgenic mouse, wherein the agent modulates a phenotype associated with a disruption in a lymphoid-specific GPCR gene.

29. The method of claim 28, wherein the phenotype comprises cellular infiltration in any one of the following organs: lung, pancreas, stomach or liver.

30. The method of claim 29, wherein the cellular infiltration is comprised of lymphocytes.

31. A method of identifying an agent which modulates lymphoid-specific GPCR expression, the method comprising:

(a) providing a cell comprising a disruption in a lymphoid-specific GPCR gene;

(b) contacting the cell with the agent; and

(c) determining whether the agent modulates lymphoid-specific GPCR gene expression, wherein the agent modulates a phenotype associated with a disruption in a lymphoid-specific GPCR gene.

32. The method of claim 31, wherein the phenotype comprises cellular infiltration in any one of the following organs: lung, pancreas, stomach or liver.

33. The method of claim 32, wherein the cellular infiltration is comprised of lymphocytes.

34. A method of identifying an agent which modulates lymphoid-specific GPCR gene function, the method comprising:

(a) providing a cell comprising disruption in a lymphoid-specific GPCR gene;

(b) contacting the cell with an agent; and

(c) determining whether the agent modulates lymphoid-specific GPCR gene function, wherein the agent modulates a phenotype associated with a disruption in a lymphoid-specific GPCR gene.

35. The method of claim 34, wherein the phenotype comprises cellular infiltration in any one of the following organs: lung, pancreas, stomach or liver.

36. A method of identifying an agent which modulates a phenotype associated with a disruption in a lymphoid-specific GPCR gene, the method comprising:

(a) administering an agent to a transgenic mouse comprising a disruption in a lymphoid-specific GPCR gene; and

(b) determining whether the agent modulates the phenotype.

37. The method of claim 36, wherein the phenotype comprises cellular infiltration in any one of the following organs: lung, pancreas, stomach or liver.

38. An agent identified by the method of claim 25, claim 28, claim 31, claim 34 or claim 36.